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Overweight and obese poorly controlled severe asthma patients have increased levels of gut permeability biomarkers lipopolysaccharide-binding protein (LBP) and calprotectin

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The human gut microbiota appears to represent an important contributor to asthma severity which may be worsened by obesity [(1)]. It appears weight gain changes gut microbiota composition and may increase intestinal permeability, leading to gram-negative bacterial fragments, referred to as lipopolysaccharides (LPS) entering the circulation[(2)]. This increase in LPS may exacerbate the systemic inflammatory response in patients with asthma and obesity. However, it is currently unclear whether intestinal permeability biomarkers (IPBs) such as lipopolysaccharide-binding protein (LBP) and calprotectin are directly influenced by weight gain and influence severe asthma. This study therefore examined the relationship of IPBs on asthma severity and weight gain, to determine the potential influence of the intestinal barrier as a target for future dietary therapy. Fasted blood was collected from patients, in an ethically approved study (REC#: 14/WM/1226), with severe asthma into the Wessex AsThma CoHort of difficult asthma (WATCH) (women: n = 69; age: 46.42 ± 14.60yrs; BMI: 32.34 ± 7.48Kg/m^2; men: n = 29; age: 52.72 ± 16.08yrs; BMI: 29.16 ± 5.69Kg/m^2; all on high dose inhaled corticosteroids). Circulating LBP, calprotectin and inflammatory markers were assessed by ELISA. Patients completed the Asthma Control Questionnaire-6 (ACQ-6), and scores were used to assess the relationship between gut permeability markers and asthma control. Descriptive statistics, group comparisons with one-way-ANOVA (AN), Kruskal-Wallis (KW) or Mann Whitney (MW) tests and simple linear regression test were conducted to compare the association between BMI, ACQ-6 score and gut permeability markers.

Simple linear regression was used to investigate the relationship between gut permeability and inflammatory markers. Circulating levels of LBP and calprotectin were significantly increased in obese patients with severe asthma (BMI:>30; LBP: 17.06 ± 8.35μg/mL#; calprotectin: 996.14 ± 659.30ng/mL*) compared with lean patients with severe asthma (BMI: 18.5-24.9; LBP: 11.36 ± 4.27μg/mL#; calprotectin: 541.77 ± 357.93 ng/mL*; #P < 0.001 *P < 0.01. Circulating LBP levels were significantly raised in patients with poorly controlled asthma (ACQ-6 score ≥1.5) compared with patients with well controlled asthma (LBP: 15.10 ± 7.88 μg/mL vs 10.95 ± 4.50μg/mL; P = 0.0279). Furthermore, irrespective of asthma control, LBP was raised in obese patients (LBP: 17.06 ± 8.35μg/mL) compared with either overweight (LPB: 11.83 ± 6.68 μg/ml) or lean patients (11.36 ± 4.27μg/ml; P = 0.0004). Significant positive correlations were identified between increasing levels of LBP with asthma-related cytokines granzyme A (P < 0.05); granzyme B (P < 0.05); and CCL4 (P < 0.05). Rising level of calprotectin was also positively correlated with granzyme A (P < 0.005). Concentrations of LBP and calprotectin were not influenced by gender or age. In summary, increased levels of gut permeability markers were associated with poorer asthma control, increased body weight, and increasing inflammatory markers of asthma. These data therefore suggest that assessment of systemic LBP and calprotectin levels in subjects with asthma and obesity may offer insight into disease severity. Furthermore, the role of these intestinal permeability markers suggests that the intestinal barrier could be the target of future dietary interventions to improve disease management.

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References

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